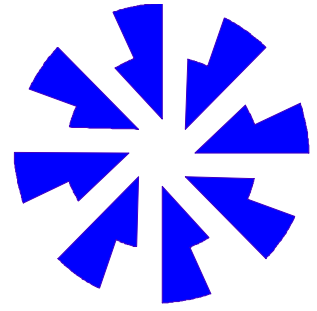




GETINGE A.B.

Technical Information Data Sheet

Specification for Getinge cGMP Equipment Features

TECHNICAL INFORMATION DATA SHEET

Specification for Getinge cGMP Equipment Features

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The Getinge Group

Disinfection and Sterilization Business

Getinge is a world leading company in the field of medical technology, specializing in the development and manufacture of equipment for the HealthCare and Pharmaceutical industries.

With over sixty years of experience, and manufacturing plants in Sweden, United Kingdom, United States, France and Australia, we are the World's leading supplier of disinfection and sterilization equipment, serving customers in more than 100 countries on all 5 continents.

Getinge manufactures a full range of steam and gas sterilizers. We produce a wide range of "industry standard" models and offer a custom design and build service for special products and applications.

Always at the forefront of sterilization technology, we are constantly developing new features and techniques to satisfy the demands of our customers and regulatory bodies.

We pride ourselves in our world - class, market leading technology, employing every aspect of our exhaustive experience and 'know-how' to solve our clients' problems in the sterilization of the new delivery and packaging systems for pharmaceuticals and medical devices.

Introduction

As the World's leading manufacturer of sterilization equipment for the Pharmaceutical Industry, Getinge A.B. accepts a responsibility to promote the state-of-the-art in sterilization technology.

There are few rules and regulations that define cGMP in terms of technical specification. Indeed most sterilizers produced by Getinge will satisfy those regulations that do exist and in this respect, most Getinge sterilizers comply with GMP requirements.

However, for those customers who require an additional assurance to be at the leading edge in terms of cGMP compliance, Getinge offers an additional, optional, package of equipment features that address all current concerns in the industry.

Working from experience gained over many years, we have developed this set of equipment features designed to satisfy the known cGMP requirements of the Pharmaceutical Industry - including those of Europe, U.S. and Japan.

Scope

This document refers specifically to steam sterilizers (Getinge reference GE), steam and air mixture sterilizers (Getinge reference GEV) and circulating water sterilizers (Getinge reference GEC).

As required, comments are added to distinguish between features specific to each model.

Definitions

The '**Product**' is defined as the item or items being processed in the sterilizer.

The '**Process System**' is defined as any part of the chamber or piping system that is in contact with the product, or in contact with media that is subsequently in contact with the product during a sterilization process.

Generally, this includes all pipework connected to the sterilizing chamber, up to and including the first isolation valve and all lines carrying process media (steam, water or filtered air) to the chamber.

'**Control sensor**' is defined for the purpose of this document as the sensor that activates the timer for Exposure Period.

'**Exposure period**' is defined as the holding period after the Control Sensor has achieved sterilization temperature.

Comments in parentheses [] are specifically for customer consideration.

'**Dead-leg**' is defined as any pipe or connection in the Process System in which there is no flow, that is greater than six (6) times the internal diameter of the pipe.

Chamber and Piping System

Materials - Chamber

The chamber shall be manufactured from Stainless Steel type 316¹. All components, fittings & fixings used within the chamber shall be stainless steel of a grade appropriate to the product, process and media. Generally, Stainless Steel type 304 shall be acceptable for this application.

Materials - Piping and components

The Process System piping and components shall be fabricated using piping of a material suitable for the application. The process media shall not be contaminated by the materials and materials shall not be corroded by the process media.

Generally, Stainless Steel type 316¹ shall be used for applications where Clean or Pure steam is used as the Process Media.

Drainage

The piping & components in the Process System shall be designed to drain freely - either into the chamber (and from there to waste), or directly to the waste system. No pipes or connections shall be allowed, or have the ability to collect or hold water or condensate. [Consideration shall be given to the steam supply to ensure it is adequately drained.]

The piping system shall be designed, and equipment selected and installed such that pipes, fittings and components do not retain moisture

Piping shall be sloped to a minimum of 1% towards the drain (e.g. 3 mm fall in a 300 mm length)

Backflow prevention

Means shall be provided to prevent backflow of one medium into another at interconnections between systems, and from the drain system to the Process System.

¹ Type 316 'L' or 'Ti' , etc according to local practice or requirements

Dead-Legs

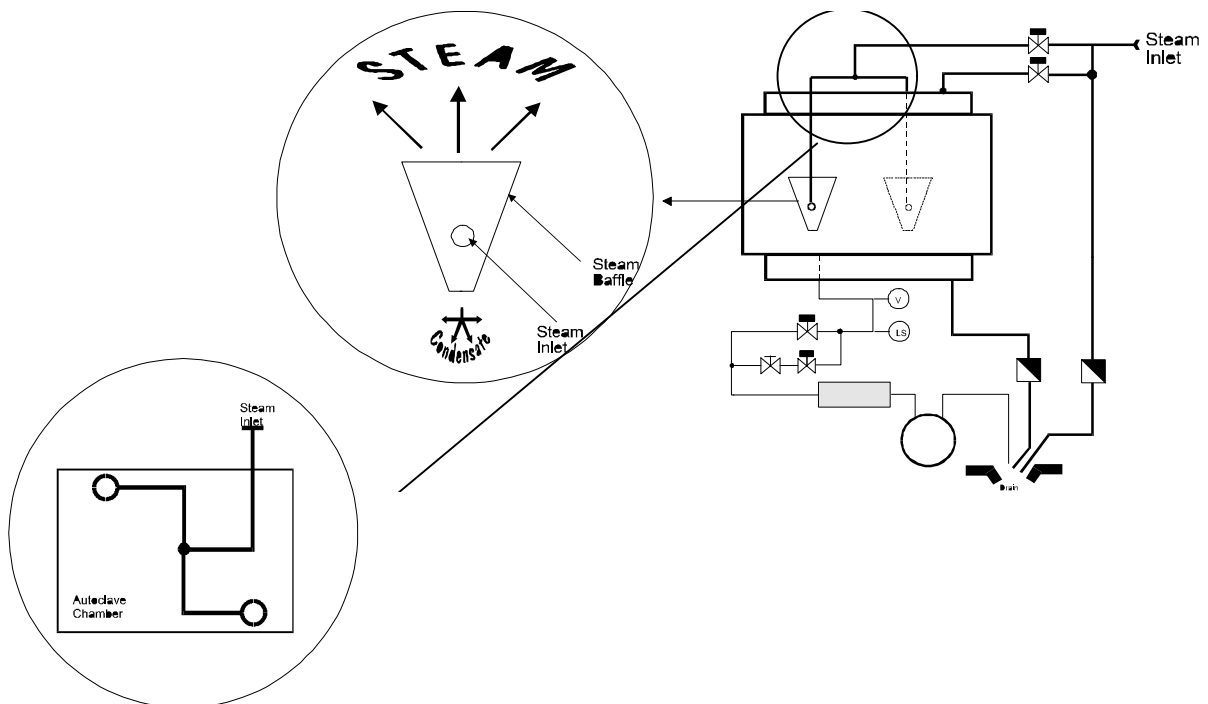
There shall be no Dead Leg in the Process System

All Process System piping and components shall be designed to be sterilized as part of each process cycle (or otherwise be sealed during process cycles in which it is not used).

Consideration shall be given to lines and connections that are be used infrequently or are unused during an alternate process. (For example, steam inlet manifolds on GEC type sterilizers fitted with a vacuum sterilizing capability, and vice-versa, water inlet manifolds on the same equipment). In such cases, the use of bleeders and/or maintenance sanitization cycles shall be used.

Steam Inlet

Steam inlet piping and manifolds shall be designed and constructed to distribute steam uniformly throughout the chamber.



Air Inlet

Air entering the chamber shall be filtered if the air is subsequently in contact with the Product.

Air inlet filters for vacuum break and admission of compressed air shall be a microbial retentive membrane filter. The pore size of the

filter shall be according to specific regulatory and product requirements, but shall generally be less than 0.22 µm.

GEV and GEC

Heat Exchangers

Internal Heat Exchanger - GEV

The internal heat exchangers shall be of sanitary design and fabricated from the same material as the chamber (usually Stainless Steel type 316¹) and designed to negate the possibility of leakage of coolant into the chamber or Process System.

The heat exchanger system / control system shall incorporate a Leak Test program to periodically check the integrity of the Heat Exchangers.

External Heat Exchanger - GEC

The external heat exchangers shall be of sanitary design with process contact surfaces fabricated from the same material as the chamber (usually Stainless Steel type 316¹) and designed to negate the possibility of leakage of coolant into the chamber or Process System.

Generally, where a plate heat exchanger is used, it shall incorporate a dual gasket system.

¹ Type 316 'L' or 'Ti', etc according to local practice or requirements

Validation Ports

A minimum of one test connection for the entry of thermocouple temperature sensors shall be fitted in an accessible location.

As a guide, one port for each two load modules shall be provided. Each load module is 1.0 to 1.3 m deep. This is subject to practicality to be assessed in each case.

Connection shall be a minimum of 50 mm diameter to accept a minimum of 12 thermocouple sensors.

Insulation

[All pipes operating above 60°C, or carrying cold water shall be insulated. However, it may be impractical to insulate all pipes in this definition. As a guide, pipes greater in length more than 10 times their external diameter(10D) shall be insulated. Generally, incoming water lines shall be insulated up to the first point of use. In most cases, insulation is only practical after installation of the sterilizer.]

Cleaning

Internal surfaces of the chamber shall be smooth and crevice free. The surfaces shall be polished to provide a minimum Ra value of 0.63 µm. Internal corners shall be radiused with a minimum 50 mm radius.

The internal surface of the door shall have a surface finish similar to the internal surface of the chamber.

The internal surface of chamber ports (nozzles) shall have a surface finish similar to the internal surface of the chamber.

Fascia and Bioseal Panels

It shall be possible to clean the front surfaces of the fascia and bioseal panels.

[All gaps between fixed panels and all gaps between the fascia and the adjacent walls / floor shall be filled with suitable sealant after installation on site.]

All areas behind fascia panels shall be accessible for cleaning. Where required for access for cleaning, or for access for maintenance, fascia panels shall be hinged to open.

Internal Chamber Fitments

Loading Rails and Equipment fitted to chamber

It shall be possible to remove internal loading equipment fixings (rails, rollers) for periodic cleaning and maintenance.

Strainers

All chamber drain ports shall be fitted with a removable mesh strainer to prevent debris from entering the chamber drain piping. (The mesh shall be removable from inside the chamber for routine cleaning by the machine operator.)

Internal Liner (GEV)

The internal liner of the GEV sterilizer shall be removable for cleaning.

There shall be no hidden areas that are inaccessible.

Internal Distribution Plate (GEC)

The internal distribution of the GEC sterilizer shall be removable for cleaning.

GEV
and
GEC

Control System

GE
and
GEV

Temperature Control

Chamber Temperature will be controlled on a temperature or pressure basis according to cycle and product requirements. In either case, the Exposure Period shall be controlled according to temperature - the lowest temperature of the chamber environment and product.

For non-liquids cycles, this will generally be according to the Chamber Drain temperature only (it is assumed, and verified during qualification, that the chamber drain is the coolest part of the chamber).

For liquids, where the liquid volume is greater than 100 ml, the exposure period shall be controlled according to chamber drain and load temperature.

By default, Exposure Period control shall always be by Chamber Drain, and if fitted, Load Temperature sensors.

GEC

Temperature Control

Chamber Temperature will be controlled according to the temperature of the circulating water. Exposure Period shall be controlled according to temperature - the lowest temperature of the product sensors fitted.

GE
and
GEV

Condensate Control

A bleed valve (drain valve by-pass) shall be installed in the chamber drain line. This shall be opened during the heating and exposure phases to eliminate condensate.

The bleed ensures a steady flow of steam across the control and verification sensors.

Means shall be provided to detect a blockage of the bleed valve. High condensate level shall activate an alarm within the control system, but shall not abort the process. If the temperature at the control sensor is depressed by the presence of condensate, the process shall automatically abort.

Pressure Instruments

Pressure gauges, transducers and other capillary lines connecting instrumentation to the chamber, shall comply with the Dead Leg' requirement above. If impractical, pressure transmitting liquid filled diaphragm or electronic transducer systems shall be used.

In case of use of electronic systems relying on an electric power supply, for safety, a mechanical gauge (also complying with this specification) shall be fitted in the service area.

Process Recorder

As a minimum, temperature and pressure values shall be recorded on a time base during each process cycle. This shall be independent of the control system or designed to indicate differences between the controlled and recorded values. This recorder may be included in the optional Cycle Printer' detailed below.

Reference Instrument

Independent reference instruments (verification sensors) shall be fitted to monitor temperature sensors and pressure sensors controlling the process.

The verification sensors shall be independent of the control system in respect of the actual sensor, excitation circuits, amplifiers and scaling and calibration.

For non-liquids cycles, the verification temperature sensor shall be a second RTD sensor located in the chamber drain pipework (the Chamber Drain sensor may be dual element - one element connected to the controller and the other to the monitoring system).

For liquid cycles, a dual element load temperature sensors is required. One element of the probe shall be connected to the controller, and the other shall be connected to the monitoring system.

A verification pressure sensor is required.

Temperature Sensor Accuracy

This shall be according to local codes and practices.

Generally Pt100 RTD sensors according to IEC 751, and with an accuracy better than $\pm 0.2^{\circ}\text{C}$ shall be used.

Alarm Systems

These shall be designed to continuously monitor conditions that are critical to the sterilization process in order to ensure personnel safety, equipment safety and product quality and integrity.

All alarms that occur during a process shall be recorded. The system shall register concurrent alarms.

Alarms shall include audible and visual indicators. Means to silence audible alarms shall be provided. Silencing the audible alarm shall not cancel the visual alarm, until the alarm is acknowledged or cleared. When silenced for one alarm, the audible alarm shall remain active for other alarms.

Alarms are segregated into three types:

Fatal - those which cause the process to stop. Operator to decide whether the cycle shall be continued or aborted. These include, but are not limited to:

- Intentional abort by operator - operation of 'Stop' button
- Power failure for more than pre-set time
- Time-out of process or equipment critical phases - where process efficacy would be affected or equipment damage would occur
- Failure of temperature and pressure sensors.
- Door lock failure (loss of 'closed' or 'locked' indication)
- Pump Failure (COS ~~Ø~~ pump monitor system error)
- Fan Failure (COS ~~Ø~~ fan watch system error)

Non-fatal - those which allow process to continue. These include, but are not limited to:

- High condensate level detected
- Interlock test errors

GEC

GEV

Optional Items

Cycle Printer

An automatic measurement and recording system shall be provided. The following data and parameters shall be recorded, as a minimum:

Header, including:

Date	Sterilizer I.D.
Load Identification	Operator I.D. & Signature
Cycle Start Time (real time)	Cycle Type selected

Cycle Parameters:

Value of adjustable parameters
Set sterilizing time and temperature

Logged on adjustable time base:

Chamber pressure	Load temperature(s) (note 2)
Chamber Drain Temperature (note 1)	Verification sensor values (note 3)

Note 1: Applies to Non-Liquids cycles only.

Note 2: Applies to Liquids cycles only.

Note 3: See Reference Instrument'below.

The sterilizer & process I.D. shall be identified at the top of each page of the process log such that the specific process run can be uniquely identified. Phase changes within the process shall be indicated.

PACS Supervisor

The PACS Supervisor is a combination Reference Instrument and Process Recorder.

The PACS Supervisor is provided with independent sensors for temperature and pressure. These are then the 'Verification Sensors' mentioned above.

The verification sensors shall monitor the control sensors and may indicate an alarm if the sensors deviate by more than a pre-set limit during the process.

The values of the control temperature sensors, verification sensors and pressure sensor shall be combined in a data acquisition system (i.e. on a single data printout). All alarms shall be noted in the documentation.

In-situ Air Filter Sterilization (AFS)

This applies to microbial retentive air filters in a stainless steel housing, used for vacuum break or admission of compressed air to the chamber. When AFS is specified:

A cycle shall be provided to automatically sterilize the filter element within the housing. The piping system upstream of the filter, to the first isolating valve, shall be sterilized as part of each process.

It shall be possible to record and validate each cycle. The process record shall indicate and report its satisfactory completion.

The drain of the filter housing and/or upstream piping is equipped with a temperature sensor (Control Sensor), and the cycle is operated according to a sequence for a gravity displacement sterilization cycle, with an added cooling phase. See separate sheet for detailed description.

In-situ Air Filter Integrity Test (AFT)

This applies to microbial retentive air filters in a stainless steel housing, used for vacuum break or admission of compressed air to the chamber. When AFT is specified:

A cycle shall be provided to automatically test the integrity of the filter element within the housing.

It shall be possible to record and validate each cycle. The process record shall indicate and report its satisfactory completion.

The filter housing shall be equipped with a pressure sensor and ancillary equipment to enable a forward flow pressure decay, water intrusion test, or similar, to be performed.

The control system shall indicate 'Pass' or 'Fail' on termination. The test shall be designed according to procedures and parameters specified by the filter manufacturer. The filter manufacturer shall provide approval in writing of the test parameters and procedure.

Sanitary Piping system (SAN)

When specified, this will be provided in conjunction with stainless steel Process System piping. All piping and components in the Process System shall be of sanitary specification.

The features of a 'sanitary' system include:

- The system shall be completely self draining, and shall not retain moisture. The 'system' includes all components, fittings and piping in the Process System.
- The system shall be free of crevices where dirt might accumulate. Internal surfaces shall be cleanable. Optionally, the chamber shall have a higher grade surface finish - E.P. or high mechanical polish (e.g. Ra=0.2µm).
- When connections can be avoided, the components shall be welded in place. However, consideration is given to removal of components and assemblies for cleaning and inspection.
- Connections shall be made using approved (to 3A or IDF standard) sanitary style fittings, such as tri-clamps. Screwed connections shall not be used.
- Valves shall be of sanitary design, such as diaphragm type valves. Globe valves shall not be used.

Optional items for Sanitary Specification

- ◆ Material specifications and mill sheet certificates may be provided for piping and components (in Getinge's Extended Documentation package).
- ◆ Weld Records may be provided.
 - ◇ Weld samples shall be produced before and after the machine construction to indicate repeatable performance of the welding equipment.
 - ◇ Welds shall be identified by reference number (e.g. engraving or sketch)
 - ◇ Welds shall be inspected by video boroscope indicating reference numbers as above.
 - ◇ Welding equipment parameters should be printed and included in the weld documentation.